Medical Policy:

Signifor® LAR (pasireotide)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.23	February 18, 2025	October 8, 2019

Definitions

Signifor® LAR is an injectable cyclohexapeptide somatostatin analog. Pasireotide exerts its pharmacological activity via binding to somatostatin receptors (SSTRs). There are five known human somatostatin receptor subtypes: SSTR 1, 2, 3, 4, and 5. These receptor subtypes are expressed in different tissues under normal physiological conditions. Somatostatin analogs bind to SSTRs with different potencies. Pasireotide binds with high affinity to four of the five SSTRs.

Length of Authorization

Coverage is provided for 6 months and may be renewed

Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

Acromegaly

- 60 billable units (60 mg) every 28 days

Cushing's disease

- 40 billable units (40 mg) every 28 days

Dosing and Administration

Indication	Dose
Acromegaly	Initiate at 40 mg administered by intramuscular injection once every 4 weeks (28 days). – Titrate dosage based on treatment response and tolerability up to maximum 60 mg every 4 weeks for patients who have not normalized GH and/or IGF-1 levels after 3 months of treatment with the 40 mg dose.
Cushing's Disease	Initiate at 10 mg administered by intramuscular injection once every 4 weeks (28 days). – Titrate dosage based on treatment response and tolerability up to maximum 40 mg every 4 weeks for patients who have not normalized 24-hour urinary free cortisol (UFC) after 4 months of treatment with the 10 mg dose.

Guideline

INITIAL CRITERIA

1. **Acromegaly**
   A. Patient diagnosis confirmed by elevated (age-adjusted) or equivocal serum IGF-1 as well as inadequate suppression of growth hormone (GH) after a glucose load; **AND**
   B. Patient has documented inadequate response to surgery and/or radiotherapy or it is not an option for the patient; **AND**
   C. Patient's tumor has been visualized on imaging studies (i.e., MRI or CT-scan); **AND**
   D. Baseline GH and IGF-1 blood levels have been obtained (renewal will require reporting of current levels); **AND**
   E. Previous failed trial or contraindication to a somatostatin analogue (e.g., octreotide [Sandostatin® LAR], lanreotide [Somatuline® Depot]) and a dopamine agonist (e.g., bromocriptine, cabergoline)
   F. Will not be used in combination with oral octreotide or with GH-analogues (e.g., pegvisomant)

2. **Cushing's Disease**
   A. Confirmed diagnosis of endogenous Cushing's disease in which the patient's hypercortisolism is not a result of chronic administration of high-dose glucocorticoids or other physiologic conditions; **AND**
   B. Treatment of patient's disease with pituitary surgery has not been curative OR the patient is not a candidate for pituitary surgery; **AND**
   C. Baseline 24-hour urinary free cortisol (UFC) level, Adrenocorticotropic hormone (ACTH), late-night salivary cortisol (LNSC), and/or serum cortisol level have been obtained (renewal will require reporting of current levels)

RENEWAL CRITERIA

1. Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in Initial Criteria; **AND**
2. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: uncontrolled hyperglycemia, diabetes, ketoacidosis, bradycardia, QT prolongation, liver test elevations (e.g., alanine aminotransferase [ALT] or aspartate aminotransferase [AST]), cholelithiasis (gallstones) and complications of cholelithiasis (e.g., cholecystitis or cholangitis), pituitary hormone (e.g., thyroid, adrenal, gonadal) deficiencies/severe adrenal insufficiency, etc.; **AND**

   Acromegaly

   A. Disease response as indicated by an improvement in signs and symptoms compared to baseline; **AND**
      i. Reduction of growth hormone (GH) by random testing to < 1.0 mcg/L; **OR**
      ii. Age-adjusted normalization of serum IGF-1

   Cushing's Disease

A. Disease response indicated by reduction in urinary free cortisol (UFC), plasma adrenocorticotropic hormone (ACTH), late-night salivary cortisol (LNSC), and/or serum cortisol levels from baseline

Limitations/Exclusions

1. Pasireotide (Signifor LAR) is not considered medically necessary for conditions other than acromegaly/Cushing's disease and when the criteria above are not met.
2. Safety and effectiveness of Pasireotide (Signifor LAR) have not been established in pediatric patients (< 18 years of age).
3. Patient must not have severe hepatic impairment (i.e., Child-Pugh Class C)

Applicable Procedure Codes

Code	Description
J2502	Injection, pasireotide long acting, 1 mg

Applicable NDCs

Code	Description
55292-0139-01	Signifor LAR 10mg Suspension Reconstituted
00078-0748-81	Signifor LAR 10mg Suspension Reconstituted ER
00078-0641-81	Signifor LAR 20mg Suspension Reconstituted ER
55292-0140-01	Signifor LAR 20mg Suspension Reconstituted ER
00078-0741-81	Signifor LAR 30mg Suspension Reconstituted ER
55292-0141-01	Signifor LAR 30mg Suspension Reconstituted ER
00078-0642-81	Signifor LAR 40mg Suspension Reconstituted ER
55292-0142-01	Signifor LAR 40mg Suspension Reconstituted ER
00078-0643-81	Signifor LAR 60mg Suspension Reconstituted ER
55292-0143-01	Signifor LAR 60mg Suspension Reconstituted ER
55292-0134-01	Signifor LAR 10mg Vial
55292-0135-01	Signifor LAR 20mg Vial (ea)
55292-0136-01	Signifor LAR 30mg Vial (ea)
55292-0137-01	Signifor LAR 40mg Vial (ea)
55292-0138-01	Signifor LAR 60mg Suspension Reconstituted ER

ICD-10 Diagnoses

Code	Description
E22.0	Acromegaly and pituitary gigantism
E24.0	Pituitary-dependent Cushing's disease

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	2/18/2025	Annual Review: Removed E34.4, no criteria changes

EmblemHealth & ConnectiCare	1/8/2024	Annual Review: adding length of authorization, dosing limits, updated dosing and administration, added renewal criteria, AddedL "Patient does not have severe hepatic impairment (i.e., Child-Pugh Class C)" to limitations and exclusions
EmblemHealth & ConnectiCare	5/9/2023	Annual Review: Guideline (Initial Criteria) removed "1.Pasireotide (Signifor LAR) is considered medically necessary for patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative OR Patients with a diagnosis of acromegaly when all-of the following criteria are met: a.Inadequate response to surgery and/or surgery is not an option b.Previous failed trial or contraindication to a somatostatin analogue (e.g., octreotide [Sandostatin® LAR], lanreotide [Somatuline® Depot]) and a dopamine agonist (e.g., bromocriptine, cabergoline) c.Signifor LAR is prescribed/recommended by an endocrinologist" Added "Acromegaly † A.Patient diagnosis confirmed by elevated (age-adjusted) or equivocal serum IGF-1 as well as inadequate suppression of growth hormone (GH) after a glucose load; AND B.Patient has documented inadequate response to surgery and/or radiotherapy or it is not an option for the patient; AND C.Patient's tumor has been visualized on imaging studies (i.e., MRI or CT-scan); AND D.Baseline GH and IGF-1 blood levels have been obtained (renewal will require reporting of current levels); AND E.Previous failed trial or contraindication to a somatostatin analogue (e.g., octreotide [Sandostatin® LAR], lanreotide [Somatuline® Depot]) and a dopamine agonist (e.g., bromocriptine, cabergoline) F.Will not be used in combination with oral octreotide or with GH-analogues (e.g., pegvisomant) 2. Cushing's Disease † A.Confirmed diagnosis of endogenous Cushing's disease in which the patient's hypercortisolism is not a result of chronic administration of high-dose glucocorticoids or other physiologic conditions; AND B.Treatment of patient's disease with pituitary surgery has not been curative OR the patient is not a candidate for pituitary surgery; AND C.Baseline 24-hour urinary free cortisol (UFC) level, Adrenocorticotropic hormone (ACTH), late-night salivary cortisol (LNSC), and/or serum cortisol level have been obtained (renewal will require reporting of current levels)" Added Codes E34.4 and E24.0
EmblemHealth & ConnectiCare	10/04/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	04/17/2020	Added under Limitations/ Exclusions per FDA Label: Safety and effectiveness of Pasireotide (Signifor LAR) have not been established in pediatric patients (< 18 years of age).
EmblemHealth & ConnectiCare	10/08/2019	Under Guideline added Pasireotide (Signifor LAR) is considered medically necessary for patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative

References

1. Signifor LAR prescribing information. Novartis. East Hanover, NJ. Reviewed October 2019.
2. Specialty-matched clinical peer review.